Immunoprophylaxis against respiratory syncytial virus (RSV) with palivizumab in children

Immunoprophylaxis against respiratory syncytial virus (RSV) with palivizumab in children: a systematic review and economic evaluation

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Executive summary

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Executive summary

Background

Respiratory syncytial virus (RSV) causes outbreaks of respiratory tract infection in the winter months in the UK. It is the leading cause of lower respiratory tract infection (LRTI) in infants and can lead to hospitalisation, particularly in those who are premature or who have chronic lung disease (CLD) or congenital heart disease (CHD). There are currently two licensed specific therapies in the UK: ribavirin and palivizumab. Palivizumab is a monoclonal antibody designed to provide passive immunity against RSV and thereby prevent or reduce the severity of RSV infection. It is licensed for the prevention of serious lower LRTI caused by RSV in children at high risk. While it is recognised that a policy of using palivizumab for all children who meet the licensed indication does not meet conventional UK standards of cost-effectiveness, most clinicians feel that its use is justified in some children. The purpose of this review is to determine if we can identify subgroups in whom palivizumab is cost-effective.

Objective

This review aims to systematically examine the scientific evidence about the effectiveness and cost-effectiveness of palivizumab for the prevention of RSV in children and to look at prognostic factors to determine if it is possible to identify subgroups among which there are important differences in cost-effectiveness.

Methods

We systematically reviewed the literature about the effectiveness and cost-effectiveness of prophylaxis with palivizumab. Bibliographic databases were searched from inception to March 2007 with no date limits or language restrictions. Current economic evaluations were analysed to identify which parameters were driving the different cost-effectiveness estimates. A probabilistic decision-analytical model was built to assess the cost-effectiveness of prophylaxis with palivizumab for children at risk of RSV infection and the parameters populated with the best available estimate thought to be most applicable to the UK context. Data to inform parameters in our model were systematically sought from the identified trial data and pragmatically identified from observational studies in the wider literature. Meta-analyses were carried out where appropriate.

Results

Clinical effectiveness

Two randomised controlled trials (RCTs) were identified. Prophylaxis with palivizumab for preterm infants without CLD or children with CLD resulted in a 55% reduction in RSV hospital admission: 4.8% (48/1002) in the palivizumab group and 10.6% (53/500) in the no prophylaxis group ($p = 0.0004$).

Prophylaxis with palivizumab was associated with a 45% reduction in RSV hospitalisation rate among children with CHD. Hospitalisation rates for RSV were 5.3% (34/639) in the palivizumab group and 9.7% (63/648) in the no prophylaxis group ($p = 0.003$). A slightly higher mortality in the control group was found in both RCTs, but this was not statistically significant. However, the trials were not powered to demonstrate a difference. Palivizumab had a relatively safe adverse event profile.

Cost-effectiveness

Existing economic evaluations

Three systematic reviews and 18 primary studies were identified. All the systematic reviews stated that the potential costs of palivizumab were far in excess of any likely savings achieved by decreasing hospital admission rates, and that the use of palivizumab was unlikely to be cost-effective in all children for whom it is recommended, but that continued use of palivizumab for particularly high-risk children may be justified. The incremental cost-effectiveness ratios (ICERs) of the primary studies varied 17-fold for life-years gained (LYG), from £25,800/LYG to £404,900/LYG, and several hundred-fold for quality-adjusted life-years (QALYs), from £3200/QALY to £1,489,700/QALY for preterm infants without CLD or children with

CLD. For children with CHD, the ICER varied from £5300/LYG to £7900/LYG and from £7500/QALY to £68,700/QALY.

An analysis of what led to the discrepant ICERs showed that the assumed mortality rate for RSV infection was the most important driver. The rates of hospital and paediatric intensive care unit (PICU) admissions and sequelae of RSV also had measurable effects.

Birmingham Economic Evaluation (BrumEE)

We undertook an independent economic evaluation. The resource use and unit cost were obtained from the trial studies, *British National Formulary* (BNF), Office for National Statistics (ONS), Economic and Social Research Council (ESRC) and previous economic evaluation studies. The utilities were obtained from a UK cohort study. Cost-effectiveness analyses were undertaken from both NHS and societal perspectives. Estimates from an NHS perspective derived using different methods confirm that palivizumab does not reach conventional levels of cost-effectiveness in any of the licensed indications if used for all eligible children – the lowest ICER being £64,000/QALY.

When additional risk factors for RSV hospitalisation derived from observational studies (gestational age, age at the start of the RSV season, having siblings who are in day care or at school) were modelled using the BrumEE, prophylaxis against RSV infection with palivizumab was within the willingness-to-pay threshold of £30,000/QALY in a number of important subgroups of children with CLD. There was insufficient data to undertake a similar risk group analysis for children with CHD.

Conclusion

Prophylaxis with palivizumab is clinically effective for reducing the risk of serious LRTI caused by RSV infection and requiring hospitalisation in high-risk children, but if used unselectively in the licensed population the ICER is over £60,000/QALY, which is double that considered to represent good value for money in the UK (the current willingness-to-pay threshold is about £30,000/QALY). The BrumEE shows that prophylaxis with palivizumab may be cost-effective (based on a threshold of £30,000/QALY, but the threshold for decision-makers may vary, particularly for this type of patient group) for children with CLD when the children have two or more additional risk factors.

Our economic evaluation is limited by the quality and quantity of the primary data available and the pragmatic rather than systematic methods used to identify parameter values. Future research should initially focus on reviewing systematically the major uncertainties for patient subgroups with CLD and CHD (e.g. mortality rates for RSV infection in children not given palivizumab prophylaxis) and then on primary research to address the important uncertainties that remain.

Publication

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The research findings from the HTA Programme directly influence decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC). HTA findings also help to improve the quality of clinical practice in the NHS indirectly in that they form a key component of the 'National Knowledge Service'.

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